

## FDCA And Liability For State Failure-To-Warn Claims

*Law360, New York (January 25, 2010)* -- Federal law requires pharmaceutical manufacturers to obtain approval for drug products from the U.S. Food and Drug Administration prior to marketing. See Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 et seq.

Pursuant to the FDCA, a manufacturer must show that the product is safe and effective for use under the conditions prescribed, recommended or suggested in the proposed labeling. 21 U.S.C. § 355, FDCA 52 Stat. 1040. Likewise, FDA approval for the labeling on pharmaceutical products must be obtained prior to marketing. *Id.*

Under common law in most states, a manufacturer is liable when the product label fails to give an adequate warning of injury known to result from use of the product. These tort suits are known as failure-to-warn actions.

Since the FDA regulates the content of labels on pharmaceutical products, can a manufacturer be held liable for the content of the label? The United States Supreme Court addressed the issue of whether the FDCA preempts state failure-to-warn claims in *Wyeth v. Levine*, 129 S.Ct. 1187, 173 L.Ed. 2d 51 (2009).

Since the *Levine* decision issued, the Eighth Circuit and a number of district courts have considered whether preemption depends upon whether the drug is a brand (approved after submission of a New Drug Application ("NDA")) or a generic (approved after submission of an Abbreviated New Drug Application ("ANDA")).

In *Levine*, the U.S. Supreme Court considered whether the filer of an NDA is liable for injury that could have been avoided had there been an adequate warning on the label. The Supreme Court held that the FDCA does not preempt state claims for a failure-to-warn based either on a theory of impossibility or on a theory of the frustration of congressional intent.

In reaching this holding, the court considered the legislative history, the purpose of the FDCA and whether it was the "clear and manifest purpose of Congress" to supersede state law.

After reviewing the legislative history of the act, and the amendments made to the act over the years, the court found that "[a]s it enlarged the FDA's powers to 'protect the public health' and assure the safety, effectiveness and reliability of drugs, Congress took care to preserve state law." *Id.* at 1195–6.

The court concluded "[e]vidently, [Congress] determined that widely available state rights of action provided appropriate relief for injured consumers." *Id.* at 1199.

The court rejected *Wyeth's* argument that under the FDCA, the FDA — not the manufacturer — bears primary responsibility for drug labeling. Rather, the court found that "a central premise of federal drug regulation [is] that the manufacturer bears the responsibility for the content of its label at all times." *Id.* at 1197–8.

The court was likewise not persuaded by Wyeth's argument that irrespective of congressional intent, it was impossible to comply with both federal and state law because federal regulations do not allow a manufacturer to alter its drug label without prior FDA approval. The court disagreed, identifying 21 CFR § 314.70(c)(b)(iii)(A)(C), known as the "changes being effected" ("CBE") regulation.

Under the CBE, a drug manufacturer may make labeling changes relating to safety after it submits the proposed change to FDA, but prior to receiving FDA approval for the change. That is, while Wyeth did have to file its proposed labeling changes, it did not have to wait for FDA approval to change the label to add a safety warning.

The court concluded that unless Wyeth could provide clear evidence that FDA would not have approved a change in the label, Wyeth could both comply with its duty to warn and adhere to FDCA requirements. *Id.* at 1198.

Since the Supreme Court's decision in *Levine* issued on March 4, 2009, the Eighth Circuit and several district courts<sup>[1]</sup> have issued opinions addressing whether the FDCA preempts a generic company's liability for a failure-to-warn under state law. In each of these cases, all parties agreed that the patient had taken only the generic drug product.

In some, the brand was a named defendant and the plaintiffs argued that any liability for failure-to-warn rested with the NDA holder ("the brand") because the Hatch-Waxman Amendments to the FDCA require the ANDA holder to have a label identical in nature to the NDA holder's label. 21 USC § 355 (j)(2)(v); 21 CFR § 314.94(a)(8).

These attempts to hold the brand liable for the injury caused by the generic equivalent were unsuccessful.

"[T]he imposition of liability on brand name manufacturers for injuries caused by competitor generic manufacturers is inconsistent with Oklahoma law, precedents from other jurisdictions and sound public policy ... [T]here is no legal support for plaintiffs' attempt to extend liability to manufacturers who did not distribute the product to [the plaintiff]." *Schrock v. Wyeth*, 601 F.Supp.2d 1262, 1266–67 (D.Ok., 2009).

The generic companies contended that their cases could be distinguished from *Levine* and, therefore, the Supreme Court's holding in *Levine* did not apply to them.

The generic companies argued that the issue raised in their cases was not whether the FDCA preempts state claims as it was in *Levine*, but rather whether the Hatch-Waxman Amendments preempt state claims. See e.g. *Kellogg v. Wyeth*, 612 F.Supp.2d 437–441 (D.Vt., 2009).

According to defendant generic companies, the Hatch-Waxman Amendments barred them from adding warnings not found on the brand label. Since they could not comply with state law if federal law requires their label to mimic that of the brand, the generic companies concluded, the Hatch-Waxman Amendments preempted state failure-to-warn claims.

In *Mensing v. Wyeth*, 588 F.3d 603 (8th Cir., 2009), the Eighth Circuit reversed a district court's pre-*Levine* finding of preemption based upon the Supreme Court's decision in *Levine*. The court found that FDA regulations required generic applicants to comply with 21 CFR § 314.70, regulating labeling, including the CBE process. *Mensing* at 611.

The Eighth Circuit dismissed the argument that the Hatch-Waxman Amendments — not the FDCA as a whole — provided the relevant statutory framework. The Eighth Circuit concluded that the analysis set out in *Levine* for brand companies applies equally to generic companies.

"[A]dditions to the statute like the Hatch-Waxman Amendments must be considered part and parcel of the FDCA. These amendments provided for cheaper, expedited approval of generic drugs, not relief from the fundamental requirement of the FDCA that all marketed drugs remain safe." Mensing at 612.

The Eighth Circuit was equally unpersuaded by the argument that state failure-to-warn claims obstruct the purpose of the Hatch-Waxman Amendments because they would require companies filing ANDAs to perform expensive studies.

The court pointed out that while labeling changes need to be scientifically supported, there is no requirement that generic companies run such studies. See 21 CFR § 314.94.

When there is reasonable evidence that a drug is associated with a serious hazard, "21 CFR § 201.57(e) does not permit generic manufacturers passively to accept the adequacy of their drug's label as they market and profit from it." Mensing at 609.

With the exception of *Gaeta v. Perrigo Pharmaceuticals Co.*, 2009 WL 4250690 (N.D.Cal., 2009), all of the district court opinions issued since *Levine* comport with the Eighth Circuit's holding that the FDCA, as amended by the Hatch-Waxman Amendments, does not preempt state failure-to-warn claims.

The district courts have found that the FDCA does not bar manufacturers from changing a drug's label after the ANDA was approved. "[G]eneric manufacturers, like brand manufacturers, can invoke § 314.70 to strengthen their warnings, *Levine* is fully applicable to generic manufacturers." *Munroe v. Barr Laboratories Inc.*, 2009 WL 4047949 \*2 (N.D.Fla., 2009).

The district courts rejected the argument that the CBE regulations apply only to the brand. The CBE regulations are found in 21 C.F.R. § 314, Subpart B (titled "Applications") and applicable to the NDA holders.

FDA regulations located at 21 C.F.R. § 314, Subpart C (titled "Abbreviated Applications") and applicable to ANDA holders require "the applicant [to] comply with the requirements of §§ 314.70 and 314.71 regarding the submission of supplemental applications and other changes to an approved abbreviated application." 21 C.F.R. § 314.97.

Since the CBE regulations are located at the 21 C.F.R. § 314.70, the courts reasoned, the CBE regulations apply equally to ANDA holders. See e.g. *Bartlett v. Mutual Pharmaceutical Co.*, 2009 WL 3126305 (D.N.H., 2009). The district courts further determined that the Hatch-Waxman Amendments do not evidence congressional intent to alter state product liability law. *Id.*

The only post-*Levine* district court that did not apply the holding of *Levine* to generic manufacturers was the Northern District of California.

Following the Supreme Court's decision in *Levine*, the plaintiff in *Gaeta v. Perrigo Pharmaceuticals*, 2009 WL 4250690 (N.D.Cal., 2009), moved for reconsideration of the district court's earlier decision that the FDCA preempts state failure-to-warn claims.

The district court's initial decision had been based upon the regulation that labels proposed in ANDAs must be substantially the same as that of the brand (21 U.S.C. § 355(j)(2)(A)(v)) and FDA's remark in the Federal Register following a revision to 21 C.F.R. § 314.70 that "CBE changes are not available for generic drugs approved under an [ANDA] ... To the contrary, a generic drug manufacturer is required to conform to the approved labeling for the listed drug." *Gaeta*, 2009 WL 4250690 \*3, quoting 73 Fed. Reg. 2848, 2849 n.1.

The court found the Levine decision did not impact its decision that failure-to-warn claims are preempted because Levine applied to branded drugs, not to generics. Other district courts have declined to give FDA's introductory remarks published in the Federal Register the force of law.

"Had the FDA intended that, notwithstanding the clear language of § 314.97, the CBE provision was nevertheless inapplicable to drugs approved via ANDAs, one would have expected § 314.97 — or the CBE provision itself — to contain language to that effect or, at least, for the FDA to have clearly explained, in enacting those provisions, that a generic manufacturer could not use the CBE process to change its labels. But, FDA did none of these things." Bartlett, 2009 WL 3126305 at \*16 (D.N.H., 2009).

Based on the district court decisions that have issued since the Supreme Court's decision in Levine, it would be prudent for generic companies to monitor adverse-impact results and safety studies done on any drug product they market.

If there is reasonable evidence that a safety issue is associated with the drug product, the generic company should file a change in label via the CBE procedure, 21 CFR § 314.70(c)(6)(iii)(A)–(D). The CBE should be filed to avoid a generic company's liability for state failure-to-warn claims, irrespective of the brand's position.

--By Elizabeth A. Leff, Frommer Lawrence & Haug LLP

*Elizabeth Leff is a partner in the Washington, D.C. Office of Frommer Lawrence & Haug.*

*The opinions expressed are those of the author and do not necessarily reflect the views of Frommer Lawrence & Haug LLP or Portfolio Media, publisher of Law360.*

[1] *Mensing v. Wyeth*, 588 F.3d 603 (8th Cir., 2009); *Schrock v. Wyeth Inc.*, 601 F.Supp.2d 1262 (W.D.Oklahoma, 2009); *Kellogg v. Wyeth*, 612 F.Supp.2d 437 (D.Vermont, 2009); *Stacel v. Teva Pharmaceuticals USA*, 602 F.Supp.2d 899 (N.D.Illinois, 2009); *Couick v. Wyeth*, Civ. Action No. 3:09–00210 (W.D.North Carolina, 2009); *Gaeta v. Perrigo Pharmaceuticals Co.*, 2009 WL 4250690 (N.D.Cal., 2009); *Bartlett v. Mutual Pharmaceutical Co.*, 2009 WL 3126305 (D.N.H.)